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NEWS EXPRESS October 14 CURRENT WINDOWS VERSION IS V6.01,
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T3 116 GIL E /AU

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L4 1 SENUT M

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\Rightarrow s 11 and 13

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ACCESSION NUMBER: 97306894 EMBASE

DOCUMENT NUMBER: 1997306894

TITLE: The use of nonneuronal cells for gene delivery.
AUTHOR: Snyder E.Y.; Senut M.
CORPORATE SOURCE: E.Y. Snyder, Department of Neurology/Pediatrics, Harvard Medical School, Children's Hospital, 300 Longwood Avenue, Boston, MA 02115, United States
SOURCE: Neurobiology of Disease, (1997) 4/2 (69-102).
Refs: 217
ISSN: 0969-9961 CODEN: NUDIEM
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
LANGUAGE: English

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L6 0 S L1 AND L3

=> s hormone (s) receptor (s) dimer

L7 1015 HORMONE (S) RECEPTOR (S) DIMER

=> s l1 and l7

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L9 0 L3 AND L7

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High level transactivation by a modified Bombyx ecdysone receptor in mammalian cells without exogenous retinoid X receptor.

Suhr ST, Gil EB, Senut MC, Gage FH.

Laboratory of Genetics, The Salk Institute for Biological Studies, 10010
North Torrey Pines Road, La Jolla, CA 92037, USA.

Our studies of the *Bombyx mori* ecdysone receptor (BE) revealed that, unlike the *Drosophila melanogaster* ecdysone receptor (DE), treatment of BE with the ecdysone agonist tebufenozide stimulated high level transactivation in mammalian cells without adding an exogenous heterodimer partner. Gel mobility shift and transfection assays with both the ultraspiracle gene product (Usp) and retinoid X receptor heterodimer partners indicated that this property of BE stems from significantly augmented heterodimer complex formation and concomitant DNA binding. We have mapped this "gain of function" to determinants within the D and E domains of BE and demonstrated that, although the D domain determinant is sufficient for high affinity heterodimerization with Usp, both determinants are necessary for high affinity interaction with retinoid X receptor. Modified BE receptors alone used as replication-defective retroviruses potently stimulated separate "reporter" viruses in all cell types examined, suggesting that BE has potentially broad utility in the modulation of transgene expression in mammalian cells.

PMID: 9653129 [PubMed - indexed for MEDLINE]

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1: Mol Ther 2000 Feb;1(2):159-64

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Adenovirus-mediated inducible gene expression in vivo by a hybrid ecdysone receptor.

Hoppe UC, Marban E, Johns DC.

Institute for Molecular Cardiobiology, Johns Hopkins University, Baltimore, Maryland 21205, USA.

Precise control of transgene expression would markedly facilitate certain applications of gene therapy. To regulate expression of a transferred gene in response to an exogenous compound in vivo, we modified the ecdysone-responsive system. We combined the advantages of the Drosophila (DmEcR) and the Bombyx ecdysone receptor (BmEcR) by creating a chimeric Drosophila/Bombyx ecdysone receptor (DB-EcR) that preserved the ability to bind to the modified ecdysone promoter without exogenous retinoid X receptor (RXR). In cultured cells, DB-EcR effectively mediates ligand-dependent transactivation of a reporter gene at lower concentrations of the chemical ecdysone agonist GS-E than VgRXR (DmEcR + RXR). Transgene delivery in vivo was achieved by intramyocardial injection of recombinant adenovirus vectors in adult rats. Upon stimulation with GS-E, DB-EcR potently (>40-fold induction) activated gene expression in vivo while VgRXR was not induced. This hybrid ecdysone receptor represents an important new tool for in vivo transgene regulation with potentially diverse applications in somatic and germline transfer.

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